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EXAMINER	
QAZI, SABIHA NAIM	
ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/671,138	SHAH ET AL.	
	Examiner	Art Unit	
	SABIHA QAZI	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-14* is/are pending in the application.

4a) Of the above claim(s) *8-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *8-13* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Final Office Action

Claims 1-6 and 8-14 are pending. No claim is allowed.

Summary of this Office Action

1. 35 USC § 103(a) Obviousness Rejection
2. Data in the specification
3. Response to Remarks
4. Conclusion
5. Communication

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be *obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patent ability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patent ability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35

U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6 and 14 are rejected under 35 U.S.C. 103(a) as obvious over SUNSHINE (US Patent 4,486,436), TENCZA et al. (US Patent 4,943,565), Remington's Pharmaceutical Sciences Page 1837, SCHROEDER et al. (US Patent 6,602,520) and JAIN et al. (WO 01/87264).

Applicant Claims

A solid pharmaceutical dosage form comprising caffeine, a disintegrant selected from the group consisting of sodium starch glycolate,

crosslinked carboxymethylcellulose, and mixtures thereof, and a cephalagic, wherein said caffeine is in the form of uncoated ungranulated particles having a granular morphology and an average particle size of about 70 to 600 microns, and wherein at least 86 % of said caffeine dissolves within 5 minutes, when measured by USP, Type II Apparatus (Paddles) set at 50 rpm.

Determining the scope and contents of the prior art (MPEP 2141.01)

SUNSHINE (US Patent 4,486,436) teaches analgesics and anti-inflammatory compositions comprising caffeine (3,7-dihydro-1,3,7-trimethyl-1H-purine-2,6-dione) and novel analgesic and anti-inflammatory compositions for use in eliciting an analgesic or anti-inflammatory response, said compositions comprising caffeine together with a selected non-narcotic analgesic/non steroidal anti-inflammatory drug or a selected narcotic analgesic, or both. When used in combination with the selected drugs, **caffeine enhances** the analgesic or anti-inflammatory response and also hastens its onset (see the abstract). The reference teaches a composition of selected non-narcotic analgesics/non steroidal anti-inflammatory drugs, which differ substantially in chemical structure from aspirin, phenacetin and acetaminophen, and which have significantly different biological profiles therefrom, can be advantageously formulated into novel pharmaceutical

compositions together with c**affeine** and administered to mammals, especially humans, to not only elicit a more potent analgesic or anti-inflammatory response but also to evoke such response more rapidly than possible by administration of the analgesic or anti-inflammatory agent alone. See lines 44-55 in column 6. Suitable disintegrators can include, without limitation, starch, methylcellulose, agar, bentonite, cellulose, wood products, alginic acid, guar gum, citrus pulp, **carboxymethylcellulose** and sodium lauryl sulfate. See lines 34-60 in column 21. See the entire document especially lines 1-36 in column 5, lines 24-32 in column 6, examples and claims.

TENCZA et al. teaches tablets containing, in combination, aspirin, acetaminophen and caffeine having improved dissolution rates. The combination of aspirin, acetaminophen and caffeine is popular in analgesic preparations and finds widespread use, particularly in over-the-counter (O.T.C) products. Tencza teaches 4-19% of caffeine (claims 1 and 9), about 30mg to about 130mg of caffeine (claim 7), about 9% to 11% of caffeine by weight (claim 6). Moreover, a widely used dosage form for delivering this combination drug is tablet. Since these products are also likely to be subjected to elevated temperatures while in storage in warehouses and in

homes, it has become customary in course of manufacturing such tablets to store them at elevated temperatures for extended periods of time to test their stability and the in-vitro availability of the active ingredients; i.e., **aspirin, acetaminophen and caffeine** for pharmaceutical action. One method for measuring the latter has been to measure the dissolution rates of the tablets. If the tablets meet a certain standard for dissolution rate, the active ingredients should be available for absorption into the blood stream within an acceptable period of time after ingestion.

The dissolution rate is adjusted such that at least 75% of the tablet dissolves in 45 minutes (lines 31-36 in column 6). The dissolution rates of tablets containing aspirin, acetaminophen and caffeine can be improved by incorporating a low-substituted hydroxypropylcellulose in sufficient amount to serve as a secondary disintegrant. See the entire document especially abstract, lines 5-40 in column 3, examples and claims.

Remington's Pharmaceutical Sciences reference teaches clearly teaches that disintegrants is a substance or a mixture of substances, added to a tablet to **facilitate its breakup or disintegration after administration**. It teaches materials serving as disintegrating agents which include cellulose and crosslinked polymers. It teaches **sodium starch glycolate as disintegrant.**

It further teaches that factors other than the presence of disintegrants can effect significantly the disintegration time of compressed tablets. The binder, tablet hardness and the lubricant have been shown to influence the disintegrate time.

SCHROEDER et al. teaches rapidly disintegrating preparations containing at least one active pharmaceutical ingredient and at least one excipient can be obtained. It teaches ibuprofen, caffeine and disintegrating agent carboxymethylcellulose. See the entire document especially abstract, line 20-30 in column 3, line 1 in column 4, lines 3-13 in column 5.

JAIN et al. teaches a rapidly disintegrating solid oral dosage form of a poorly active ingredient particles have an average diameter, prior to inclusion in the dosage form of less than about 2000 nm. The dosage form of the invention has the advantage of combining rapid dissolution. The reference teaches the nanoparticulate size of less than 1500, less than 1000, less than 600 etc. The rapid disintegration time is lass than 3 minutes, 2 minutes, 90 seconds (see lines 1-25 on page 8). See the entire document especially abstract, section A on page 6, page 7, and 8, section C. on page 11, section 4 on page 13, section B on page 14, section C. on page 17.tables and claims.

Ascertaining the differences between the prior art and the claims at issue (MPEP 2141.012)

Presently claimed invention differs in claiming specific solubility.

Finding of Prima Facie Obviousness, Rational and Motivation obviousness or nonobviousness (MPEP 2142-2143)

It would have been obvious to one skilled in the art at the time the invention was made to prepare additional beneficial solid pharmaceutical compositions having good dissolution rate and synergism containing active and useful drugs in combination **with caffeine and a disintegrant** because prior art teaches that by the addition of caffeine synergistic results are obtained and second disintegrant is added to improve the dissolution rate. Applicants' composition does not contain any weight or amounts of caffeine or any other ingredients neither any temperature of dissolution measurement is in claims. The dissolution of caffeine is expected to depend on the quantity of caffeine present in the solid composition and temperature. Motivation to dissolve the desired percentage (claimed at least 86% or 95%) has been provided by both the references cited above and the disintegrant carboxymethylcellulose is taught by SUNSHINE. Furthermore, Remington's Pharmaceutical Sciences clearly teaches that disintegrants is a substance or a mixture of substances, added to a tablet to facilitate its breakup or disintegration after administration. It teaches materials serving as disintegrating agents which include cellulose and crosslinked polymers. It teaches sodium starch glycolate as disintegrant. It further teaches that factors other than the presence of disintegrants

can effect significantly the disintegration time of compressed tablets. The binder, tablet hardness and the lubricant have been shown to influence the disintegrate time. CHROEDER teaches the preparation of rapidly disintegrating tablets containing at least one active pharmaceutical ingredient and at least one excipient can be obtained. It teaches ibuprofen, caffeine and disintegrating agent carboxymethylcellulose. No unexpected results are noted. Since the amount of caffeine is not given in claims the dissolution of caffeine cannot be compared with the prior art. JAIN teaches the particle size composition of poorly soluble drugs and the dissolution rate of less than 90 seconds of nanoparticulates of less than 1500nm (see pages 14-17. The reference also teaches granular form; see part 3 on page 15.

There has been ample motivation to prepare the composition of caffeine with rapid disintegration containing various particle sizes, because Sunshine teaches disintegrants is a substance or a mixture of substances, added to a tablet to facilitate its breakup or disintegration. The disintegration is expected to depend on amount of disintegrant present in the tablet and the temperature at which the dissolution rate is measured. The disintegrant **sodium starch glycolate** tablet will provide rapid disintegrating by using the same ingredients and teaches all the factors which influence the disintegration such as the temperature and the quantities of the ingredients therefore, at the time the invention was filed it would have been obvious to prepare such tablets.

Data in the specification

The specification discloses that "The surfaces of the caffeine particles according to the invention are substantially free, preferably free, of polymeric binders and coating materials. One commercially available form of such caffeine may be obtained from BASF under the designation anhydrous caffeine granular, 0.2/0.5. The dosage form is solid. In one embodiment, the dosage form is a compressed tablet or caplet. The dosage form may also be uncoated or coated with conventional coating materials", (see lines 3-8 on page 3 of the specification).

It appears that the caffeine particles are said to be "substantially free" of polymeric binders coating materials. **Substantially free** is not defined. It may contain some coating. In the example disclosed in present specification there is no ungranulated and uncoated caffeine used. No criticality and/or unexpected results are noted.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

Response to Arguments

Applicants' response filed on 2/28/11 is hereby acknowledged.

Applicant's arguments were fully considered but are not found persuasive therefore all the rejections are maintained.

Applicant argues (page 2 of remarks) that:

> Applicants have previously noted (*see* Applicants' response dated August 27, 2010) superior dissolution rates found when uncoated ungranulated particles of caffeine having a granular morphology and an average particle size of about 70 to 600 microns are included in a solid pharmaceutical dosage form.
>
> Applicants maintain that the proposed combination of Sunshine et al., Tenceza et al., Remington's Pharmaceutical Sciences, and Schroeder et al., do not disclose or suggest the inclusion of uncoated ungranulated particles of caffeine having a granular morphology and an average particle size of about 70 to 600 microns.
>
> Thus, it is respectfully submitted that if one skilled in the art were to combine Sunshine et al., Tenceza et al., Remington's Pharmaceutical Sciences, and Schroeder et al. as proposed, the resulting solid pharmaceutical dosage form may possibly exhibit a dissolution rate where at least 75% of the caffeine-acetaminophen tablet dissolves in under 45 minutes.

Examiner disagrees because (1) amount of caffeine in the composition is not disclosed in claim 1 of the present invention. Applicant's claims are drawn to specific caffeine particle size and at least 86% and 95% of the said caffeine dissolves within 5 minutes. It is unclear what is amount of caffeine is in the composition, from which 86% will dissolve within 5 minutes and there is no mention of the temperature. Applicants are comparing/arguing the prior art dissolution without explaining the basis. If the amount of caffeine is present in

very small quantity of it will dissolve much faster than large quantities. There is no mention of the amounts of any component present in the claimed composition including caffeine. Tencza teaches 4-19% of caffeine (claims 1 and 9), about 30mg to about 130mg of caffeine (claim 7), about 9% to 11% of caffeine by weight (claim 6). Present claims have no quantities of components. Temperature of the measurement of dissolution is also missing. The solubility will increase with the temperature. Tencza also teaches the use of the same apparatus i.e. USP paddle Type II. The paddle rotation is 50rpm which is the same as in present claim 1. The temperature of the experiment is maintained 37 C. Temperature is missing from present claims.

It is noted that Tencza et al. have adapted a dissolution rate such that at least 75% of the caffeine- acetaminophen tablet dissolves in under 45 minutes. (see lines Applicant argues that Tencza et al. does not teach the presently claimed invention. First of all Examiner would like to draw the attention that caffeine particles are said to be “substantially free” of polymeric binders coating materials. Substantially free is not defined. The caffeine used by Applicants is not uncoated it is "substantially free". It is not known what substantially free means. Examiner respectfully disagrees because with the arguments because the references teaches caffeine and acetaminophen tablet compositions (abstract). The caffeine is uncoated and granular with a particle size between 20 mesh to 100 mesh. The

caffeine and acetaminophen tablet also comprises a disintegrant, such as crospovidone XL-20. It is noted that crospovidone is well known in the pharmaceutical arts as crosslinked polyvinylpyrrolidone. Remington's Pharmaceutical Sciences reference teaches clearly teaches that disintegrants is a substance or a mixture of substances, added to a tablet to facilitate its breakup or disintegration after administration. It teaches materials serving as disintegrating agents which include cellulose and crosslinked polymers. It teaches **sodium starch glycolate as disintegrant.**

It further teaches that factors other than the presence of disintegrants can effect significantly the disintegration time of compressed tablets. The binder, tablet hardness and the lubricant have been shown to influence the disintegrate time.

SCHROEDER et al. teaches rapidly disintegrating preparations containing at least one active pharmaceutical ingredient and at least one excipient can be obtained. It teaches ibuprofen, caffeine and disintegrating agent carboxymethylcellulose. JAIN teaches the particle size composition of poorly soluble drugs and the dissolution rate of less than 90 seconds of nanoparticulates of less than 1500nm.

The rejection has been on combination of references. It has been decided by the court that "when the question is whether a patent claiming the combination of elements of prior art is obvious", the relevant question is "whether the

improvement is more than the predictable use of prior art elements according to their established functions." (Id.). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." KSR v. Teleflex, 127 S.Ct. 1727, 1741 (2007). The Court emphasized that "[a] person of ordinary skill is… a person of ordinary creativity, not an automaton." Id. at 1742.

No unexpected results were noted. Prior art of record teaches the composition with the dissolution rate measured by the same apparatus. The particle size of active ingredient has been taught. Concentrations/amounts and the temperature at the time of measurement of dissolution rate of caffeine is not mentioned in claims. Solubility depends on various variables which includes temperature and concentration.

In view of the teachings of prior art presently claimed invention is considered obvious over the prior art of record for the reasons cited above.

Conclusion

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

COMMUNICATION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is (571) 272-0622. The examiner can normally be reached on any business day except Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fetterolf Brandon can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sabiha Qazi/
Primary Examiner, Art Unit 1612